

### Remarks

Claims 1, 5, 7, 12 to 16 and 19 to 21 have been amended, claims 26 to 27 are cancelled and claims 35 to 37 have been added so that claims 1 to 25 and 28 to 33 and new claims 35 to 37 are pending in this application of which only claim 1 is in independent form. Support for new claim 35 can be found, for example, in original claim 13, support for new claim 36 can be found, for example, in original claim 1 and support for new claim 37 can be found, for example, in original claim 9.

On pages 2 to 4, the Office continued to reject claims 1 to 25 and 28 to 31(34) under 35 USC §103(a) as obvious over Leipner et al., 2001 (hereinafter **Leipner**) in view of U.S. Patent 6,048,846 to **Cochran** and further in view of Friedman & Sklan (1989) and Ramussen & Seljelid (1991).

The Office expressed the opinion that Leipner teaches therapeutic use of a composition of proteolytic enzymes comprising proteolytic enzymes comprising papain, bromelain, trypsin, chymotrypsin as well as the flavonoid rutin (p. 780, col. 2, lines 19-21).

Cochran is said to teach a composition that strengthens and enhances the ability of the body to fight diseases comprising one or more amino acids, one or more enzymes, vitamins and antioxidants, and one or more minerals. The Office refers to col. 4, lines 45-56, Fig. 1, col. 16, l. 8 and 16 for the teaching of coenzyme Q-10, lycopene and  $\beta$ -carotene, vitamins C and E, selenium, L-arginine, L-glutamine, glycine, L-methionine, bromelain and papain.

Applicant has previously amended the claims to specify the hydrolases to be a combination of proteases, in particular plant/animal proteases and to further include

*Appl. No. 10/555,244  
Confirmation No. 3986  
Amendment*

one or more of the additional components recited in (a) to (c) of claim 1.

Applicant had argued earlier that Leipner provides just an overview of the use of proteases, such as bromelain, papain, trypsin and chymotrypsin and that he points out that the results obtained are often inconsistent (Abstract, fourth line from the bottom).

Applicant also argued that the secondary reference, Cochran does not mention specific enzymes such as hydrolases and certainly not animal/plant proteinases as presently claimed.

In response, the Office noted that Leipner teaches a combination of animal proteases and plant proteases and that oral therapy with proteolytic enzymes produces certain analgesic and anti-inflammatory effects. The Office also argued that the combination of proteinases disclosed seem to be advantageous in treating inflammatory processes. The Office also stated that, according to Leipner, the complexity of inflammatory processes might indicate the need for combined anti-inflammatory therapy (p. 780, col. 2, last three lines of the second full paragraph).

The Office also pointed out that Cochran teaches bromelain and papain (col. 16, l. 8 and 16) and further teaches that his composition contains 300-600 µg selenium. The Office also noted that selenium supplementation was well known in the art at the time the invention was made.

The Office expressed the opinion that it would have been obvious to one of the ordinary skill in the art to combine the composition of Leipner and Cochran to obtain a composition to strengthen the immune response and to treat inflammatory-rheumatic disorders.

The Office explained that the person of ordinary skill had good reason to pursue the known options within his/her technical grasp. The Office, in particular, expressed the opinion that because the composition as claimed has the properties predicted by

the art, it would have been obvious to make the claimed food composition.

Applicant has, as detailed below, amended the claims.

However, prior to detailing these amendments, applicant would like to emphasize that, as Leipner already states, the results obtained with enzymatic therapies are uncertain. Indeed, studies show that therapy with certain enzyme combinations have negative effects on the further development of an ailment. As an example, applicant provides the Office with a summary of a study conducted by Dörr et al. Here, a combination of papain, trypsin & chymotrypsin, was tested for the treatment of oral mucositis after radiotherapy. While the combination was well tolerated by the patients, the study revealed, after over 1 to 6 weeks, a significant difference **in favor of the placebo group**. Leipner himself reports negative effects of certain proteinases (“These findings clearly show negative effects of certain proteinases on rheumatic disorders.” (p. 781, first full paragraph)).

Thus, enzyme combinations cannot be assumed to have *per se* a positive effect. Rather, as the Dörr et al. study supports, the selection of the enzyme combination and, if appropriate, the addition of any further substance(s) has to be carefully weighted.

Claim 1 as amended now requires:

one or more plant protease, and/or  
one or more animal protease,  
(a) antioxidants comprising vitamins having antioxidant activity, and  
selenium-containing substances,  
(b) one or more flavonoids and/or one or more flavonoid-containing  
substances *[emphasis added]*.

As the Office points out, Leipner, who discloses a combination of bromelain, papain, trypsin and chymotrypsin and rutin notes that the inflammatory processes

discussed are complex and might indicate the need for combined anti-inflammatory therapy. He deduces this from research indicating that different combinations (e.g. trypsin/ rutin) were effective at certain stages of oedema development, while others where not. Leipner leaves open how these combined anti-inflammatory therapies would look like and which, if any, non-enzyme components, apart from those disclosed these combination therapies may contain.

With regard to Cochran, applicant agrees with the Office that both bromelain as well as papain are disclosed in column 16 of the patent. Notably, however, bromelain and papain are considered "Amino Acids" as described by Cochran in columns 15 and 16 and not "Enzymes" as disclosed in col. 8 and 9 of the patent. "Selenium", on the other hand, is described under the heading "Minerals". As previously noted, Cochran also defines "Enzymes" broadly to include enzymes, vitamins and antioxidants (col. 4, lines 43 to 51). Thus, Cochran's hormone, amino acid, enzyme and mineral composition differs significantly from composition currently claimed (hormones such as DHEA and melatonin are referred to as part of the composition throughout Corchran's disclosure including Fig. 1. These hormones may be administered at "supernutritional levels" (col. 5, line 10)).

While antioxidants including selenium have been used and studied as supplements, their effectiveness has been questioned repeatedly (see attached printout of about.com that summaries a 2004 AHA study on antioxidants). Selenium has indeed recently even been associated with a hightened risk for different ailments.

Applicant submits that Leipner provides a general and cautionary suggestion for a not further characterized combination therapy. While Corchoran discloses certain elements of the invention as currently claimed, he does so in a very different combination and

obviously starting from very different premises as outlined above.

Applicants submit that there was no teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention. (MPEP §2141, III (G)). However, assuming for argument's sake only, that there was a teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the Leipner and Cochran or to combine their teachings, applicant respectfully submits that a combination of these references would have given the person of ordinary skill no reason to pursue the invention as presently claimed. Applicant submits that any beneficial results obtained with the claimed combination could not have been predicted for the person of ordinary skill in the art after reading Leipner and Cochran (MPEP §2141, III (A) and (B)). Such a person could, for example, not have reasonably predicted that the stimulation of the immune system is particularly pronounced when the recited proteases are combined with selenium containing substances, flavonoids-containing substances etc. as described in the paragraph bridging pages 8 and 9 of the specification. Also, neither Leipner nor Cochran provide a finite number of identified, predictable solutions, that would have provided the person of skill in the art with a reasonable expectation of success (MPEP §2141, III (C)).

In view of the above, applicant submits that *no prima facie* case of obviousness has been established for the inventions as presently claimed.

An early issuance of a notice of allowance is therefore respectfully requested.

The Commissioner is authorized to charge any fee deficiencies or overpayment to the undersign's deposit account 50-3135.

Respectfully submitted,

/Joyce v. Natzmer/

Joyce von Natzmer  
Registration No. 48,120  
**Customer No. 46002**  
Direct Tel: (301) 657-1282

March 19, 2008

**Pequignot + Myers LLC**  
**200 Madison Ave., Suite 1901**  
**New York, New York 10016**  
**Tel: (212) 213-0135**

*Appl. No. 10/555,244*  
*Confirmation No. 3986*  
*Amendment*